Registration Decision RD2014-13

Tembotrione

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Registration Decision for Tembotrione

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Tembotrione Technical Herbicide (technical grade active ingredient) and Vios G3 (end-use product), containing the technical grade active ingredients tembotrione and thiencarbazone-methyl, to control annual broadleaved and grassy weeds in field corn.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2013-21, *Tembotrione*. Registration Decision[2] describes this stage of the PMRA's regulatory process for tembotrione and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2013-21, *Tembotrione*. This decision is consistent with the proposed registration decision stated in PRD2013-21.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2013-21, *Tembotrione* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act*"...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What is Tembotrione?

Tembotrione is an active ingredient in the end-use product Vios G3, which is a co-formulation of 350 g/L tembotrione and 70 g/L thiencarbazone-methyl. Vios G3 is a postemergence herbicide for the control of annual broadleaf and grassy weeds in field corn using ground application equipment only.

Tembotrione is a WSSA (Weed Science Society of America) Group 27 herbicide. Tembotrione inhibits the enzyme 4-hydroxyphenyl-pyruvate-dioxygenase (4-HPPD) in target plants. Inhibition of 4-HPPD disturbs chloroplast synthesis and functions. Sensitive plants exhibit symptoms in the form of strong bleaching effects, especially on the actively growing zone of shoots, and then die within two weeks.

Health Considerations

Can Approved Uses of Tembotrione Affect Human Health?

Tembotrione is unlikely to affect your health when used according to label directions.

Potential exposure to tembotrione may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100 times higher (and often much higher) than levels to which humans are normally exposed when tembotrione products are used according to label directions.

The technical grade active ingredient Tembotrione was found to be a potential dermal sensitizer and requires the statement "Potential Skin Sensitizer" on the label.

The end-use product Vios G3 was mildly irritating to the eye. For this reason, the statement

"Caution - eye irritant" is required on the label.

Tembotrione was not genotoxic. There was no evidence of carcinogenicity in the mouse. However, in long-term studies, there was evidence that tembotrione caused squamous cell carcinomas in the eye in rats due to long-term effects on that organ. There were indications that tembotrione potentially caused damage to the nervous system in rats and dogs at doses that caused other effects in test animals. The main signs of toxicity in animals given daily doses of tembotrione over longer periods of time were white areas on the eyes and keratitis-related changes to the cornea, mild haemorrhagic changes and liver, kidney and pancreatic changes. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

When tembotrione was given to pregnant animals, effects on the developing fetus were observed at doses that were toxic to the mother. However, since effects in the fetus were of a more severe nature than those seen in the mother, the fetus is considered more sensitive to tembotrione than the adult animal. Because of this observation, extra protective measures were applied during the risk assessment to further reduce the allowable level of human exposure to tembotrione.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and children 3–5 years old, the subpopulation which would ingest the most tembotrione relative to body weight, are expected to be exposed to less than 29% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from tembotrione is not of concern for all population subgroups. There were no cancer risks of concern for tembotrione.

Acute dietary (food and water) estimates for the general population and all population subgroups were less than 47% of the acute reference dose, and are not of health concern. The highest exposed subpopulation was infants less than one year old.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using tembotrione on corn were acceptable to support the domestic uses. No new maximum residue limits (MRLs) in/on corn are recommended at this time as MRLs for corn (field, sweet and pop) were previously recommended to cover residues in imported commodities. The MRLs for this active ingredient in animal commodities as a result of domestic use on field corn can be found in the Science Evaluation of the Evaluation Report ERC2012-02, *Tembotrione*.

Occupational Risks From Handling Vios G3

Occupational risks are not of concern when Vios G3 is used according to the label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Vios G3, as well as field workers re-entering freshly treated fields, can come in direct contact with tembotrione residues on the skin or through inhalation of spray mists.

Therefore, the label will specify appropriate personal protective equipment such as long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, chemical-resistant coveralls, goggles or faceshield, or engineering controls for anyone conducting specific tasks with the end-use product. In addition, restrictions on the amount of product handled per day, and restricted-entry intervals for certain postapplication activities are required. Taking into consideration these label requirements, risks to agriculture workers are not of concern.

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Tembotrione is Introduced Into the Environment?

Tembotrione is moderately to highly mobile and exhibits variable persistence in laboratory soil. Data specifically designed to investigate the extent of these properties demonstrate that it is not expected to leach significantly under field conditions in Canadian soils.

Tembotrione is toxic to small mammals, terrestrial plants, freshwater vascular plants, and estuarine/marine invertebrates. Tembotrione poses a negligible risk to earthworms, honey bees, birds, freshwater invertebrates, freshwater and marine fish, and freshwater and marine algae.

In soil, tembotrione is expected to break down in the presence of oxygen; however, in soils lacking oxygen, tembotrione is expected to persist. New information allowed for the calculation of revised half-lives and characterization of important breakdown products. Despite the relatively shorter half-lives in soil, it is still evident that tembotrione behaves quite differently depending on the soil type.

Tembotrione very easily dissolves in water. When it enters the aquatic environment, it tends to settle out of the water column and ends up in the sand or sediment. Tembotrione can persist in certain aquatic environments.

New laboratory studies indicate that tembotrione is expected to move downward through the soil, confirming previous data indicating high soil mobility. However, three additional lysimeter studies (two in Ontario and one in Quebec) showed that tembotrione did not leach significantly under Canadian field conditions. In terrestrial field studies tembotrione dissipated rapidly and did not appear to travel very deeply into the soil.

Tembotrione is not likely to breakdown by reacting with water or sunlight. Tembotrione is also unlikely to enter the atmosphere and travel long distances in air. Residues of tembotrione are unlikely to accumulate in organisms.

Tembotrione has several different breakdown products, some of which have the potential to move down through the soil, however they breakdown fairly rapidly.

Non-target organisms that may be vulnerable to adverse effects resulting from potential tembotrione exposure include terrestrial plants, freshwater aquatic plants, estuarine/marine invertebrates, and small mammals.

Value Considerations

What Is the Value of Vios G3?

Vios G3, a postemergence herbicide, is for selective control of annual broadleaved and grassy weeds in field corn using ground application equipment only.

Vios G3 at a rate of 110 mL/ha (i.e. 38.5 g a.i./ha tembotrione + 7.7 g a.i./ha thiencarbazone-methyl) is labelled for application in tank mix with Liberty herbicide (i.e. glufosinate ammonium) or glyphosate herbicide on Liberty Link (i.e. glufosinate ammonium resistant varieties) or glyphosate tolerant field corn, respectively. The tank mixes must be applied postemergence to field corn at the one- to six-leaf stage.

A single application of Vios G3 in these tank mixes provides residual control of numerous annual broadleaved and grassy weeds, including Group 2 herbicide resistant biotypes. Application of Vios G3 is compatible with integrated weed management practices and with conservation tillage and conventional crop production systems. Vios G3 is a postemergence herbicide applied after weeds have emerged. Growers can therefore better assess whether the herbicide is necessary or suitable for particular weed species. In addition, Vios G3, containing the Group 27 herbicide component tembotrione, provides Canadian corn growers with an alternative weed management tool to control weeds that have developed resistance to other herbicide modes of action.

Vios G3 also contains thiencarbazone-methyl, a WSSA Group 2 herbicide, which inhibits the enzyme acetolactate synthase (ALS) in target plants. Inhibition of ALS starves the plants of essential amino acids and leading plants to chlorosis and necrosis and eventually to death.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Vios G3 to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with farmers, custom applicators, or field workers re-entering freshly treated fields coming into direct contact with Vios G3 on the skin or through inhalation of spray mists, anyone mixing, loading and applying Vios G3 must wear appropriate personal protective equipment.

The Vios G3 label specifies that anyone mixing, loading or applying the product must wear chemical-resistant coveralls and shoes plus socks. Workers mixing or loading Vios G3 must also wear chemical-resistant gloves and protective eyewear. Workers must not apply Vios G3 to more than 150 hectares per day. The Vios G3 label requires that workers do not enter treated fields for 12 hours after application.

In addition, standard label statements to protect against drift during application were added to the product label.

Environment

Due to the risks identified for tembotrione, specific mitigation measures are necessary to protect the environment. In order to protect terrestrial and nearby freshwater and estuarine/marine habitats, both aquatic spray buffer zones (1 m) and terrestrial spray buffer zones (10 m) have been determined to be necessary for tembotrione-containing end-use products. If tembotrione is applied in combination with other pesticides, the most restrictive spray buffer zones must be observed. Toxicity label statements are required for sensitive organisms including non-target plants, aquatic invertebrates, and small mammals.

Other Information

The relevant test data on which the decision is based (as referenced in Proposed Registration Decision PRD2013-21, *Tembotrione*) are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act*.